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EPIDEMIOLOGY AND CLINICAL SPECTRUM OF CUTANEOUS DISEASES MANIFESTING AMONG NEWLY DIAGNOSED HIV SEROPOSITIVE ADULTS IN NAKURU COUNTY-KENYA.

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ABSTRACT

Background. The skin is exceptionally vulnerable to various diseases in people with human immunodeficiency virus (HIV) infection. The prevalence of skin diseases in HIV varies by country and region. In Kenya, the prevalence, patterns and distribution of HIV-related skin diseases is unknown. Estimating the burden of HIV-related skin morbidity is important in planning skin care for HIV patients in any given community. It is necessary therefore to conduct such studies in Kenya.
Method. We conducted a cross-sectional survey of 394 newly diagnosed HIV seropositive patients seeking care at the HIV comprehensive care centre in Rift Valley Provincial Hospital. All patients were examined for skin diseases by two dermatologists for diagnostic concurrence. Their CD4 cell counts were analysed by the centre’s laboratory technologist using Fluorescence-Activated Cell Sorter (FACS) system.
Results. Women outnumbered men by 1.9:1. The overall mean age was 36.5 years (SD±9.69) and the mean CD4 cell count was 251.7cells/mm^3 (SD±261.05). 42% (166/394) of the patients presented with one or more skin diseases. Oral thrush (6.3%), pruritic papular eruption (5%), seborrheic dermatitis (4.8%), eczema (4.3%), herpes zoster (3.6%), xerosis (2.8%) and vaginal candidiasis (2.8%) were the leading diseases. Oral thrush (p<.019), pruritic papular eruption (p<.012) and seborrheic dermatitis (p<.001) were the only diseases with a significant correlation with lower CD4 cell counts.
Conclusion. Skin diseases remain common among newly diagnosed adults with HIV in Nakuru County. Most of those with skin disease are severely immunodepressed and eligible for commencement of anti-retroviral therapy.

KEYWORDS: Epidemiology, skin diseases, HIV seropositive

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INTRODUCTION

The pathologic relationship between human immunodeficiency virus (HIV) and the skin starts at seroconversion and intensifies as the CD4 cell population is progressively decimated by the virus (Cedeno-Laurent *et al.*, 2011). The skin is therefore the first and the most universally afflicted organ in the course of HIV infection (Singh *et al.*, 2009; Queiroz-Zancanaro *et al.*, 2006). Determining the burden of skin diseases among HIV patients and estimating their CD4 cell counts as well as viral loads where applicable, are therefore important components in the management of HIV related skin diseases (Jung and Paauw 1998; Ghate *et al.*, 2000). However, in underprivileged nations where expensive laboratory investigations cannot be readily afforded or conducted pronto, certain skin diseases have been used to predict initial HIV infection and immune status of most patients (Ghate *et al.*, 2000).

Majority of HIV patients live in Sub-Saharan Africa; many are undiagnosed, severely immunodepressed and suffer diverse skin problems (Maurer and Amerson, 2010). The high prevalence of HIV-related skin diseases encountered in Africa has profoundly increased the public health burden that the continent is already facing (Hu *et al.*, 2011). Epidemiologically, the prevalence and types of HIV-related skin diseases differ from country to country as well as from region to region and their patterns are known to change with time (Resneck *et al*., 2004). Due to these inevitable variations, proposals to re-categorise AIDS defining skin illnesses, to re-examine existing diagnostic criteria and to conduct further epidemiologic studies have been suggested as essential strategies to address the diversity of skin diseases observed in HIV (Resneck *et al*., 2004; Sharma *et al*. 2004; Thompson 2008).

As is common with many Sub-Saharan countries, Kenya too suffers a high HIV burden: The current HIV prevalence in Kenya is estimated to be 6.4% (6.1 - 6.9) with females (8%) outnumbering males (4%) by 2:1 (National AIDS Control Council of Kenya, 2009). Though the prevalence of HIV is known, data on HIV-related skin diseases in Kenyans are lacking or unpublished. HHhNevertheless, studies published from other Sub-Saharan countries demonstrate that HIV-related skin diseases are a major cause of public health burden in the continent (Mgonda, 2004; Josephine *et al*., 2006).

The purpose of this study was to characterise the clinical spectrum and distribution of HIV-related skin diseases among adult Kenyans with HIV and to describe their immune status. The study was conducted at the Rift Valley Provincial Hospital Comprehensive Care Centre (RVPH-CCC) which serves as an HIV care clinic for patients living within Nakuru County and its environs. HIV positive patients with diverse skin diseases are referred or refer themselves to the centre's dermatology clinic for specialist's consultation.

PATIENTS AND METHODS:

The study population was formed of newly diagnosed HIV positive patients aged eighteen years and above. Permission to conduct this study was first sought from the Rift Valley Provincial Hospital ethics committee and then from Kenyatta National Hospital/University of Nairobi Ethics Review Committee (KNH/UoN –ERC) and cleared by the National Institute for Science and Technology (NIST). Each patient's consent was sought after a thorough explanation on the purpose of the study, the procedures, potential risks and or benefits. All patients gave voluntary consent to have a full skin examination performed on them and to have censored pictures taken from them for didactic purposes.

The study was carried out from 1st February to 30th November 2012. Patients less than eighteen years old, those already on HAART and those who had been diagnosed with HIV earlier and had been receiving care elsewhere as well as pregnant women and severely ill patients were excluded from the study.

A full skin examination was performed on every patient by two dermatologists. All diagnoses were made on clinical grounds. Due to financial constraints biopsies were not done on cases which could not be diagnosed clinically instead such cases were categorised as "uncertain". There were however very few of such cases. Nevertheless, investigations such as skin scrapings, VDRL (Venereal Diseases Research Laboratories) tests and pus swabs were performed where applicable. Blood for CD4 counts was drawn from each patient by a phlebotomist in the centre's laboratory and analysed using FACS machine. Mean CD4 cell count was calculated for the entire group and for each of the top ten skin diseases.

Demographic characteristics such as gender, age, and marital status were recorded for each patient. These, together with the diagnosis and CD4 cell counts of each patient were recorded on questionnaires and subsequently entered into a computer.

Data analysis was done using SPSS (Statistical Package for the Social Sciences) computer software program version 11.0 for Windows. Only descriptive statistics were done: Parameters analysed include Means, Proportions; Percentages. Prevalence of diseases was analysed by calculating the average number of patients with a particular skin disease relative to all patients participating in the study. Mean CD4 count was calculated by dividing the total number of CD4 cells with the total population under study. Relationships between skin diseases and CD4 cell counts were calculated using Chi square, a *P*-value of <0.05 was deemed significant.

RESULTS

Of the 394 patients analysed, 258(65.5%) were females and 136 (34.5%) males: 202(51.3%) of them were married while 72 (18.3%) were single; 56 (12.4%) were widows, 44 (11.2%) had been divorced and 20 (5.1%)

were separated. Their overall mean age was 36.5 (± 9.69) years: Mean ages for female and male patients were 35 and 39.5years respectfully. Table 1 shows the distribution of age and gender of the sample.

The overall mean CD4 cell count was 251.7 (SD±261.05) cells/mm^3 and ranged from 1 to 1260 cells/mm^3. Women had a comparatively higher CD4 cell counts than men— 277.4 (± 266.6) and 202.1 (±242.85) respectively.

Out of the 394 patients examined, 166 (42.1%) presented with various skin diseases: 126 (75%) of them had a single skin disease each, 33 (19.9%) had two types, 5 (3%) had three each, 1 (0.6%) patient had 4 while another one had 5 different types of skin diseases. In total, fifty five different types of skin diseases were diagnosed. The most common mucocutaneous diseases observed were as follows:- Oral thrush (6.3%), pruritic papular eruption (5%), seborrheic dermatitis (4.8%), unclassifiable eczema (4.3%), herpes zoster (3.6%), xerosis (2.8%) and vaginal candidiasis (2.8%). Table 2 and 3 shows the prevalence of skin diseases, their corresponding mean CD4 cell counts, and the relationship between skin diseases and CD4 cell counts respectively.

DISCUSSION

Majority of our patients were women (65.5%); they were also significantly younger compared to men (35years Vs 39.5 years respectively). A similar observation was made in Cameroon where female patients were the majority (61.5%) and comparatively younger (Josephine *et al.*, 2006). However, in other studies done outside Africa a predominance of men was noted (Sen *et al.*, 2009). The reason for this discrepancy is currently unknown: In the Kenyan context, the gender variance observed may reflect the national HIV prevalence where women are twice affected as men (National AIDS Control Council of Kenya 2009). It may also mean that women are more skin health conscious and do seek treatment better than men as observed in Cameroon by Josephine *et al.*, (2006).

Prevalence of skin diseases and distribution of CD4 cells

The prevalence of skin diseases in our study cohort was 42.1%, however, the number of times a diagnosis of a skin disease was made was 216 (54%). These findings compare well with those of Mohammad *et al.*, (2003) who reported a prevalence of 41.7% among HIV positive police officers in Dar es Salaam. It is however lower than the 68.8% observed by Josephine *et al.*, (2006) in Cameroon; but, unlike in our study and that conducted in Tanzania, the Cameroon study population included children.

When compared to prevalence studies done outside Africa, the prevalence in our study is much lower: In India, skin diseases affect 80% to 98% of HIV infected persons (Singh *et al.*, 2009; Sharma *et al.*, 2004). Reasons attributed to the differences in prevalence may include different study designs; the socio-economic status; the prevailing environmental conditions of different countries and the HAART status of patients under study (Maurer and Amerson, 2010; Josephine *et al.*, 2006).

In our study, oral candidiasis was the commonest disease observed; this finding is in agreement with that of Puttaiah *et al.*, (2010). Pruritic papular eruption (5%), seborrheic dermatitis (4.8%), unclassifiable eczema (3.6%), and herpes zoster (2.8%) followed in that order. These diseases are ubiquitous in advanced HIV infection and as expected they featured prominently in our study population. They have also been observed in a similar order in Thailand (Wiwanitkit, 2004) and in Tanzania (Mohammad *et al.*, 2003). It is plausible therefore, that when planning care for HIV patients, priority should be given to the five leading diseases.

Majority of our patients presented with very low CD4 counts (mean CD4 count 251.5cells/mm^3) which were distributed as follows: 71.3 % had CD4 cell count ≤ 350 cells/mm^3 (the level at or below which HAART is given in Kenya); 53% had ≤ 200cells/mm^3; 41% had ≤ 100 cells/mm^3 and 27% had ≤ 50 cells/mm^3. In comparison, the distribution of CD4 cell counts observed by Goh *et al.*, (2007) was: 63.5% had CD4 counts below 200cells/mm^3, 38.5% had counts below 50cells/mm^3 however some of their patients were already on HAART. These findings imply that majority of new patients attending the Nakuru comprehensive care clinic are HAART eligible and the many who present with severe immunodepression indict the public health management systems in the county. Health planners and practitioners ought to review the existing health campaigns strategies and prepare adequately for the high number of new HAART eligible patients consulting the Nakuru provincial hospital.

Skin diseases and their relationship with CD4 cells Counts

In our study, oral candidiasis, seborrheic dermatitis, and pruritic papular eruption were found to correlate significantly with low CD4 cell counts. This observation was also noted by Goldstein *et al.*, (1997) who reported significant relationships between the three diseases and low CD4 cell counts. Singh *et al.*, (2009) also observed a significant relationship between oral candidiasis and low CD4 counts in Bastar, India. The three diseases, especially in their most severe or atypical forms have been described as AIDS defining illnesses: They can therefore be used as clinical justifications to commence HAART in resource poor countries where CD4 cell counts are difficult to obtain.

Oral candidiasis occurring in severely immunocompromised individuals is usually florid and even atypical (Sharma *et al*., 2004). This was confirmed in our patients; majority of them had severe extensive disease involving the mouth, pharynx, larynx and oesophagus. Most of our patients with oral candidiasis had extremely low CD4 count (mean 88cells/mm^3) confirming that the disease is an opportunistic infection as was also found by Goh *et al.*, (2007). Sharma *et al*., (2004) and Puttaiah *et al.*, (2010) also found lower CD4 counts in their patients with oral candidiasis (105.28 and 150cells/mm^3 respectively). For unknown reasons, majority of our patients with oral candidiasis were females (72%); many of them had concomitant vaginal candidiasis as well as other AIDS defining medical conditions such as pulmonary tuberculosis.

The inverse relationship between seborrheic dermatitis and low CD4 cell counts observed in our study appears to be at variance with that observed by Sharma *et al.*(2004): Having not found a significant relationship between seborrheic dermatitis and low CD4 counts, the authors suggest that seborrheic dermatitis should no longer be considered an AIDS defining illness. However, seborrheic dermatitis is a disease with a wide spectrum of clinical severity ranging from simple dandruff to an erythroderma (Maurer and Amerson, (2010). Whilst mild seborrheic dermatitis occur even in the immunocompetent, severe seborrheic dermatitis is seen more frequently among HIV patients with very low CD4 cell counts (Goldstein *et al.*, (1997); Altraide (2010); Rigopoulos (2004); Mathes and Douglas 1985). Therefore, in our view, seborrheic dermatitis per se need not be expunged from the list of AIDS defining illnesses. It will make more clinical logic to first categorise seborrheic dermatitis according to its clinical severity then evaluate whether its severe forms meet the AIDS defining criteria.

Other observations

Disease free, severely immunodepressed individuals

We report three women who, despite having extremely low CD4 counts (<5cells/mm^3) did not have any skin complaint or disease. The first was a 27 years old married woman, she had a CD4 count of 1 cell/mm^3; the second was 32 years old, married, and had a CD4 count of 3cells/mm^3; and the third was 29 years old widow with a CD4 count of 4cells/mm^3. It is extremely unusual for humans with such nullity of immunity to be disease free: However, we could not ascertain for how long they had had this immunodepression before the examination neither were we able to predict how long they remained disease free afterwards.

Although this observation could have been a temporary event, it could as well mean that there are other factors which play vital roles in the preservation of our immunity besides adequate numbers of CD4 cells. Further research is warranted.

Unclassifiable eczema

Unclassifiable eczema has not frequently been classified as a common HIV-related skin disease in Africa, however, in our study, it was among the top ten HIV-related skin diseases. 70% (12/17) of our patients with unclassifiable eczema had a CD4 cell count of less than 200cells/mm^3: They all had severe, atypical and recalcitrant eczema. This observation may infer that unclassifiable eczema, especially when severe and unresponsive can be used as a predictor for both HIV positivity and decreased immunity.

To the best of our knowledge, this is the first study that classified unclassifiable eczema among the most common HIV-related skin disease in Africa. The reason(s) as to why it has not been previously reported in Africa is currently unknown; more research to address this divergence is required. However, unclassifiable eczema has been documented as a common HIV-related skin disease in countries outside Africa: Supanaranond *et al.*, (2001) and Goh *et al.*, (2007) reported unclassifiable eczema among the top ten skin diseases in Thai HIV positive patients.

Pruritic papular eruption (PPE)

Pruritic papular eruption has been described as a very common skin disease among HIV infected Africans, especially those residing in regions with high mosquito densities (Resneck *et al.*, 2004); (Goldstein et al., 1997). Its prevalence has been estimated to range from 12 – 46% [8] and has reached as high as 58% (Mgonda, 2004) in countries neighbouring Kenya. However, we found only 20 (5%) patients with PPE. Majority of our patients with PPE were female (70%) and almost all of them were severely immunocompromised (mean CD4 count 46 cells/mm^3).

Although the prevalence of PPE in our study appears to be extremely low, it is comparable to that observed by Budhavari and Grayson (2007) in South Africa. They studied biopsies of patients presenting with papular follicular eruptions and found a PPE prevalence of 6.9%. The reasons for the low prevalence rates of PPE in Kenya and South Africa as compared to other African countries are currently unclear.

Majority of PPE patients observed by Resneck *et al.*, (2004) gave positive histories of exposure to insect bites and especially mosquitoes: This observation make arthropod bites a likely aetiology for PPE. However, most of our patients denied exposure to recent mosquito bites and this could probably explain the low prevalence of PPE found in our study if as suggested it results from mosquito bites. Nevertheless, the aetiology of PPE remains controversial; recent studies suggested that PPE is seen more commonly among patients on HAART probably occurring as part of an immune reconstitution syndrome (Haddow *et al.*, 2009). If this be the case, then PPE prevalence may increase when our patients start taking HAART: More studies to this direction are warranted.

Kaposi's sarcoma

We found only one (0.25%) patient with cutaneous Kaposi's sarcoma (KS); He was 35 years old, married heterosexual man with a CD4 count of 28cells/mm^3. Although KS is rare in Africa, its prevalence in Kenya appears to be extremely low compared to 1.6% in Tanzania (Mohammad *et al.*, 2003) and 9.9% in Cameroon (Josephine *et al.*, 2006). KS occur more frequently in male homosexuals and among those infected with human herpes virus type-8 (Josephine *et al.*, 2006; Puttaiah *et al.*, 2010). While the prevalence of HHV-8 infection and males who engage in sex with other males is not known in Kenya, it is probably negligible and this may explain the paucity of KS observed in our study population.

Study limitations

The study site is a referral hospital; only patients with difficult or unresponsive skin diseases are referred to the centre. Therefore, some patients with common and easily treatable diseases may not reach the centre because they are treated in periphery centres. Our study sample was convenient and results cannot therefore be generalized to all patients with HIV living in the area. Since we examined patients only once, some patients who did not present with skin diseases during examination could have developed skin diseases later.

Implications for research and clinical practice

Further studies utilising larger sample sizes are recommended to conclusively investigate both incidence and prevalence of HIV-related skin diseases in Nakuru and other Counties in order to estimate regional and national skin health burden. Public health campaigns aimed at encouraging early voluntary HIV testing are necessary to avoid late diagnosis which inevitably is associated with advanced immunodepression. Health managers are advised to address the perennial shortage of essential dermatological drugs and of currently recommended HAART regimes in order to meet increasing demand. The number of skin specialists in Nakuru County is currently inadequate and should be increased to cope with the escalating demand for specialised skin care.

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Table 1: Age and gender distribution

Age group (years)	N(%)	F	M
18 — 27	76 (19.3)	66 (86.8%)	10 (13.2%)
28 — 37	157 (39.8%)	104 (66.2%)	53 (33.8%)
38 — 47	101 (25.6%)	59 (58.4%)	42 (41.6%)
48 — 57	52 (13.2%)	24 (46.2%)	28 (53.8%)
≥ 58	8 (2%)	5 (62.5%)	3 (37.5%)
Total	394 (100%)	258 (65.5%)	136 (34.5%)

Table 2: Prevalence of most common skin diseases and corresponding mean CD4 cell count.

DISEASE	*n* (%)	MEAN CD4 CELL COUNT(±SD)
Oral thrush	25(6.3%)	88.6(105.7)
Pruritic papular eruption (PPE)	20(5.0%)	46.6(65.2)
Seborrheic dermatitis	19(4.8%)	48(40.7)
Eczema	17(4.3%)	287.59(348.8)
Herpes zoster	14(3.6%)	318.57(225.7)
Xerosis	11(2.8%)	242.78(223.9)
Herpes genitalis	11(2.8%)	357(211.5)
Vaginal candidiasis	10(2.5%)	357(211.5)
Dermatophytosis	10(2.5%)	158.37(225.4)
Pruritus	7(1.8%)	313.0(202.3)
Total	133(33.8%)	

Table 3: Relationship between common skin diseases and CD4 count categories

DISEASE	CD4 COUNT ≤200 *n* 173	CD4 COUNT > 200 *n* 221	SIG
Oral thrush	17(9.8%)	8(3.7%)	.019
Pruritic papular eruption	14(8.1%)	6(2.7%)	.012
Seborrheic dermatitis	17(9.8%)	2(0.9%)	.001
Eczema	12(6.9%)	5(2.3%)	NS
Herpes zoster	5(2.9%)	9(4.1%)	NS
Xerosis	5(2.9%)	6(2.7%)	NS
Herpes genitalis	9(5.2%)	2(0.9%)	NS
Vaginal candidiasis	1(0.6%)	9(4.1%)	NS
Dermatophytosis	7(4%)	3(1.4%)	NS
Pruritus	2(1.2%)	5(2.3%)	NS

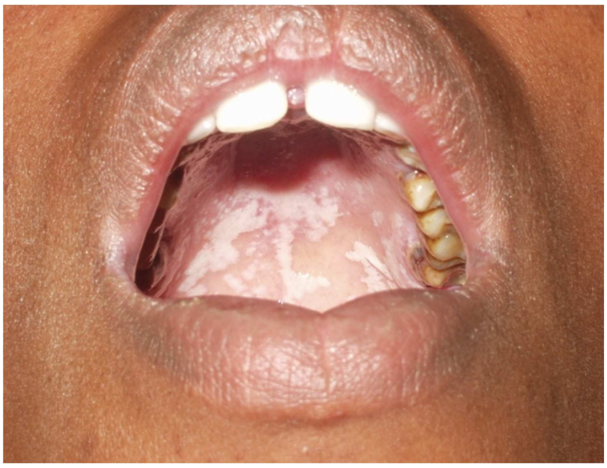

Figure 1: Oral thrush

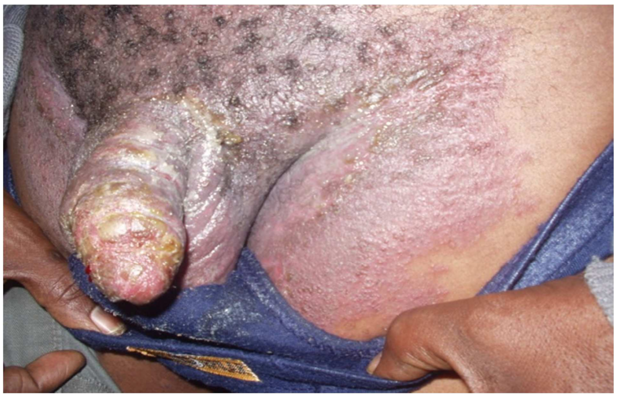

Figure 2: Seborrheic dermatitis

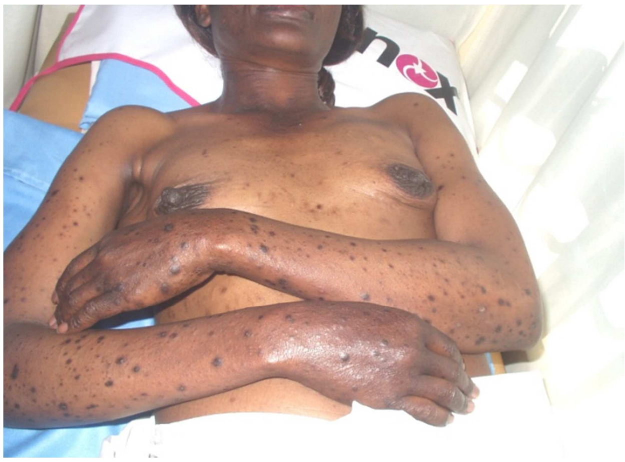

Figure 3: Pruritic papular eruption (PPE)